or a pharmaceutically acceptable salt thereof wherein:
R^1 is hydrogen, methyl or ethyl;
R^2 is a hydrocarbon radical selected from straight and branched chain alkyl of from 1-12 carbons or monocyclic aryl optionally containing 1 or more lower alkyl substituents of from 1-2 carbon atoms and/or 1 or more halogen substituents selected from Cl, F and Br;
R' is hydrogen or methyl;
R" is hydrogen or β-methyl; and
R''' is hydrogen, α-methyl or β-methyl.

37. (Amended) The transdermal skin patch according to Claim 36 wherein the 5alpha-reductase 2 inhibitor is 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one.

REMARKS

Reconsideration of this application is respectfully requested in view of the amendments above and following remarks.

Claims 28 to 37 were pending in the present application. Claims 28 to 37 have been rejected. Claims 31 and 37 have been amended. Presently, Claims 28 to 37 remain under consideration.

Claim 31 has been amended to replace the phrase "1 or more halogen (Cl, F or Br) substituents;" with the phrase "1 or more halogen substituents selected from Cl, F, and Br;". This amendment clarifies Applicants original intent in writing the claim, and does not add new matter to the present application.

Claim 37 has been amended to change its dependency from Claim 35 to Claim 36. This amendment does not add new matter to the present application.

The Examiner noted that the section heading TITLE OF THE INVENTION including the text has appeared twice in page 1 and page 19. The Examiner stated that

it was proper to delete the duplicated section heading TITLE OF THE INVENTION including the text in page 19, and requested clarification.

Applicants' copy of the present application does not have this duplication of text on pages 1 and 19. Applicants filed a Preliminary Amendment with the filing of the present application, a copy of which is enclosed with the present response. Prior to filing the Preliminary Amendment, Applicants' copy of the specification had one "TITLE OF INVENTION" section appearing at the top of each of pages 1 and 19. In the December 7, 2001, Preliminary Amendment, Applicants made the following amendments (among others):

> At p. 1, in the section labeled "TITLE OF THE INVENTION", delete the title "METHOD OF TREATING ANDROGENIC ALOPECIA WITH 5-ALPHA REDUCTASE INHIBITORS", and substitute therefor the new title – TRANSDERMAL TREATMENT WITH 5-ALPHA REDUCTASE INHIBITORS --.
>
> At p. 19, in the section labeled "TITLE OF THE INVENTION", delete the title "METHOD OF TREATING ANDROGENIC ALOPECIA WITH 5-ALPHA REDUCTASE INHIBITORS", and substitute therefor the new title – TRANSDERMAL TREATMENT WITH 5-ALPHA REDUCTASE INHIBITORS --.

Applicants' copy of the specification thus reflects deletion of the original title and addition of the new title (and no changes to the section heads). If the Examiner's copy of the present specification reads differently, Applicants authorize the Examiner to make the amendments necessary to make the Examiner's copy agree with Applicants' copy.

Information Disclosure Statement

The Examiner stated that the information disclosure statement filed March 12, 2002, failed to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each

U.S. and foreign patent, each publication or that portion which caused it to be listed, and all other information or that portion which caused it to be listed.

Applicants respectfully submit that the information disclosure statement filed March 12, 2002, was filed with all the references. As can be seen from the enclosed copy of our postcard receipt, both the PTO –1449 form and the references were received in the PTO mailroom. In order to facilitate prosecution of this application, Applicants have enclosed herewith a second set of copies of all the references originally submitted with the information disclosure statement filed March 12, 2002.

Claim Objections

Claim 37 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicants would like to thank the Examiner for pointing out their typographical error. Claim 37 has been amended to depend from Claim 36. In view of this amendment, Applicants respectfully request reconsideration and withdrawal of the objection to Claim 37.

Claim Rejections - 35 USC §112

The following is a quotation of the second paragraph of 35 USC §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31 and 37 were rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicants regard as the invention. The Examiner stated:

a. Claim 31 is indefinite since it is not clear if the halogen substituents are restricted to those set forth in the parenthetical expression. An amendment to the Claim 31 reciting "... 1 or more halogen substituents selected from the group consisting of Cl, F or Br" would obviate this rejection.

b. Claim 37 recites the limitation "the 5-alpha-reductase 2 inhibitor" in line 2. There is no antecedent basis for this limitation

in the Claim 35. An amendment to Claim 37 changing the claim dependency to Claim 36 would obviate this rejection.

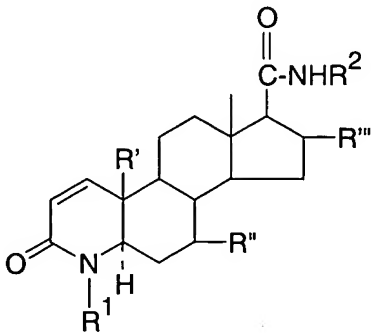
Applicants have amended Claims 31 and 37. Claim 31 has been amended to recite "1 or more halogen substituents selected from Cl, F, and Br." Claim 37 has been amended to depend from Claim 36.

In view of the amendments above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 31 and 37 under 35 U.S.C, §112, second paragraph, as being indefinite for failing to particularly point and distinctly claim the subject matter which applicants regard as the invention.

Claim Rejections - 35 USC §102

Claims 28-29 and 31-34 were rejected under 35 USC §102(b) as being anticipated by Rasmusson et al. (EP 0 285 382 A2). The Examiner stated:

> Rasmusson teaches a treatment of androgenic alopecia using 5-alpha reductase inhibitors (e.g., 17-beta-N-monosubstituted-carbamoyl-4-aza-5-alpha-androst-1-ene-3-ones). Rasmusson also teaches the limitations recited in Claims 29 and 34 (i.e., a treatment of male pattern baldness) and the species required by Claim 33 (i.e., 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one) as a preferred species, see abstract; page 2, line 47; Examples 6-12 and Claims 1-4 and 6-8. It also teaches the patented compounds having the formula found in patented Claim 1 as follows:



(wherein:

R^1 is hydrogen, methyl or ethyl;

R^2 is a branched chain alkyl of from 3-12 carbon atoms;
R' is hydrogen or methyl;
R" is hydrogen or β-methyl;
R'" is hydrogen, α-methyl or β-methyl) for the manufacture of a medicament useful for treating androgenic alopecia.

The formulas I and II required by the instant Claims 31 and 32 are encompassed by the patented formula shown above (supra). Even though the instant claims use the term "5alpha-reductase 2 inhibitor" whereas Rasmusson (EP '382) uses the term "5alpha-reductase inhibitor", they are considered to be the same or inherently same since they have same structure and utility. All the critical elements required by the instant claims are taught by the cited reference. Thus, all the claimed subject matter is rejected over the prior art of the record.

Applicants respectfully traverse the rejection of 28-29 and 31-34 under 35 USC §102(b) as being anticipated by Rasmusson et al. (EP 0 285 382 A2). The present invention is directed to a method of treating androgenic alopecia comprising transdermally administering to a person in need of such treatment a therapeutically effective amount of a 5alpha-reductase 2 inhibitor. Rasmusson EP '382 does not disclose the transdermal limitation of the present invention and does not anticipate the present invention.

In view of the remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 28-29 and 31-34 under 35 U.S.C, §102 over the Rasmusson et al. reference (EP '382).

Claim Rejections - 35 USC §103

Claims 30 and 35-37 were rejected under 35 USC §103(a) as being unpatentable over Rasmusson et al. (EP 0 285 382 A2) in view of Goldman (US 5,407,944). The Examiner stated:

> Rasmusson et al.'s teaching is mentioned in §102 rejection. For instance, the patented Claim 8 teaches various alternative topical formulations including solution, cream, ointment, gel, shampoo or aerosol. Rasmusson

teaches most elements required by the instant Claims 30 and 35-37 except a topical application being formulated in the form of a transdermal skin patch.

However, it would be obvious to one of ordinary skill in the art to make a transdermal skin patch comprising a 5α-reductase 2 inhibitor to treat androgenic alopecia (e.g., male pattern baldness) when Rasmusson's reference is modified with Goldman because Goldman suggests that a pharmaceutical preparation could be made in the form of a topical transdermal skin patch comprising a composition containing 5α-reductase 2 inhibitor (e.g., finasteride®), see Column 6, lines 10 and 20, especially line 28. Goldman teaches a method for promoting hair growth using a vasodilator in combination with estradiol and/or a 5alpha-reductase inhibitor. Since the techniques for formulating a transdermal patch is well within the skilled level of the artisan having ordinary skill in the art, one would have had the reasonable expectation of success for treating androgenic alopecia by utilizing a skin patch formulation of 5alpha-reductase 2 inhibitor as an active component taught by Rasmusson. Thus, one would have been motivated to modify Rasmusson's teaching to include a transdermal skin patch to extend the applicability and acceptance by the patient who prefers a patch application to fit their needs, wherein the increased compliance would enhance the therapeutic efficacy and achieve cost-effective treatment via short duration of therapy and because this is seen as an alternative means to deliver medications. It is noted that finasteride® is 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-en-3-one.

One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same (or similar) ingredients and share common utilities, and pertinent to the problem which applicant is concerning. MPEP 2141.01(a).

Applicants respectfully traverse the rejection of Claims 30 and 35-37 under 35 U.S.C, §103(a) over the Rasmusson et al. (EP '382) reference in view of Goldman (US '944). The Goldman patent does not suggest transdermal administration of a 5alpha reductase inhibitor including finasteride. Neither does Goldman suggest a transdermal skin patch comprising a therapeucitally effective amount of a 5alpha-reductase type 2

inhibitor including finasteride. Goldman does describe several formulations in the patent; namely:

(1) Minoxidil as a topical solution (col. 3, lines 39-52);
(2) Minoxidil in tablet form (col. 3, lines 53-62);
(3) Nitroglycerin as a transdermal system (col. 4, lines 1-6);
(4) Diazoxide as a capsule or suspension (col. 4, lines 7-18);
(5) Nifedipine as a capsule (col. 4, lines 19-38);
(6) Nifedipine as a controlled release tablet for oral administration (col. 4, lines 42-56);
(7) 17beta-estradiol as tablet or cream (col. 4, line 57 to col. 5,line 28);
(8) 17beta-estradiol as a transdermal patch (col. 5, lines 29-42);
(9) Finasteride as a tablet (col. 5, lines 43-62).

Of the nine formulations listed above from the Goldman patent, only finasteride is a 5alpha-reductase inhibitor. Minoxidil, nitroglycerine, diazoxide, and nifedipine are vasodilators under the definition of the Goldman patent, and 17-beta estradiol is an estradiol. The section of Goldman (col. 6, lines 10 and 20, especially line 28) cited by the Examiner does not teach a transdermal skin patch comprising a composition containing 5α-reductase 2 inhibitor (e.g., finasteride®), as the Examiner stated. In fact, read in context with the particular formulations Goldman teaches in the patent (cited above), Goldman teaches away from a transdermal skin patch comprising any 5alpha-reductase type 2 inhibitor, including finasteride.

In view of the remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 30 and 35-37 under 35 U.S.C, §103(a) over the Rasmusson et al. (EP '382) reference in view of Goldman (US '944).

Double Patenting

Claims 28-29 and 31-34 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent 5,547,957. The Examiner stated:

> The instant claims require an effective amount of 5alpha-reductase 2 inhibitor to treat male pattern baldness whereas US '957 teaches a therapeutically effective dosage amount from 0.05 to 3.0 mgs/day for the same treatment. Although the

conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 (US Patent '957) is directed to a method of treating male pattern baldness comprising 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one wherein male pattern baldness is androgenic alopecia, and 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one is an inhibitor or 5α-reductase 2, admitted by both patent and instant application, see US '957, Column 1, lines 14-15 and lines 50-55; and see instant Claims 2 and 33. In fact, one would have easily discovered the effective dosage required by the instant claims for treating androgenic alopecia is about 0.01 to 3.0 gms/day when the claims are read in light of specification (see page 3, line 9). It would have been obvious to one of ordinary skill in the art to expect the same result from the method required by both application and patented composition.

Applicants respectfully traverse the obviousness-type double-patenting rejection of Claims 28-29 and 31-34 over Claim 1 of U.S. Patent 5,547,957. The present application is related to U.S. 5,547,957 through a series of divisional and continuation applications, as reflected in the "CROSS REFERENCE TO RELATED APPLICATIONS" section of the present application. During the prosecution of the application resulting in the US 5,547,957 patent, there was required an election of species among (A) active agent, (B) route of administration, (C) alopecia and (D) sex of person under MPEP 809.02(D), 803. The presently claimed invention was held to be a patentably distinct invention from that claimed in US 5,547,957 in that (B) route of administration is oral in US 5,547,957 and transdermal in the present application.

In view of the remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 28-29 and 31-34 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent 5,547,957.

Claims 28 and 31-33 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 1 of U.S. Patent 5,760,046. The Examiner stated:

> Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 (US Patent '046) is directed to a method of treating female pattern baldness whereas the instant claims require the androgenic alopecia. However, the female pattern baldness is considered to be a manifestation of androgenic alopecia and encompassed by the term androgenic alopecia when this patented claim is read in light of specification (see U.S. '046, Column 1, lines 18-19 and lines 54-63). Thus, it would have been obvious to one of ordinary skill in the art to substitute female pattern baldness to androgenic alopecia as suggested in U.S. '046 patent. One would have been motivated to substitute androgenic alopecia to female pattern baldness and expected successful treatment from this substitution. Specific dosage (i.e., 0.05 to 3.0 mgs/day) is considered to be a therapeutically effective amount as mentioned earlier (supra) for treating androgenic alopecia.

Applicants respectfully traverse the obviousness-type double patenting rejection of Claims 28 and 31-33 over Claim 1 of US 5,760,046. The present application is related to U.S. 5,760,046 through a series of divisional and continuation applications, as reflected in the "CROSS REFERENCE TO RELATED APPLICATIONS" section of the present application. During the prosecution of the application resulting in the US 5,760,046 patent, there was required an election of species among A) one ultimate species of active agent inhibitor, (B) one route of administration, (C) one species of androgenic alopecia (male pattern baldness or female pattern baldness) under MPEP 809.02(D), 803. The presently claimed invention was held to be a patentably distinct invention from that claimed in US 5,760,046 in that (B) route of administration is oral in US 5,760,046 and transdermal in the present application; and (C) androgenic alopecia is female pattern baldness in US 5,760,046 and androgenic alopecia/male pattern baldness in the present application (Claim 28, 30,31,32,33,35,36,37/29,34).

In view of the remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 28 and 31-33 under the judicially created doctrine of obviousness-type double patenting as over Claim 1 of U.S. Patent 5,760,046.

For the foregoing reasons, Applicants believe that the instant application is in condition for allowance, and an early notification thereof is earnestly solicited. If the Examiner has further questions or concerns regarding this application, she is invited to telephone the undersigned attorney at the number below.

Respectfully submitted,

By _____
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Attorney for Applicants

/agb

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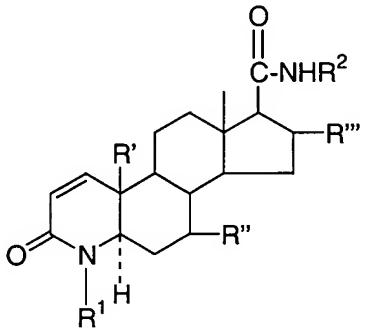
Date: October 16, 2002

Encl.: Prelim Amend, dated 12/7/01
Postcard, dated 3/7/02
References (80)

VERSION OF AMENDED CLAIMS
WITH MARKINGS TO SHOW CHANGES MADE

31. (Amended) The method according to Claim 28, wherein the 5alpha-reductase 2 inhibitor has the structural formula I:



I

or a pharmaceutically acceptable salt thereof wherein:
R^1 is hydrogen, methyl or ethyl;
R^2 is a hydrocarbon radical selected from straight and branched chain alkyl of from 1-12 carbons or monocyclic aryl optionally containing 1 or more lower alkyl substituents of from 1-2 carbon atoms and/or 1 or more halogen ~~(Cl, F or Br)~~ substituents selected from Cl, F, and Br;
R' is hydrogen or methyl;
R" is hydrogen or β-methyl; and
R''' is hydrogen, α-methyl or β-methyl.

37. (Amended) The transdermal skin patch according to Claim ~~35~~ 36 wherein the 5alpha-reductase 2 inhibitor is 17β-(N-tert-butylcarbamoyl)-4-aza-5α-androst-1-ene-3-one.